

**SUPPLEMENTAL INFORMATION****Table of Contents**

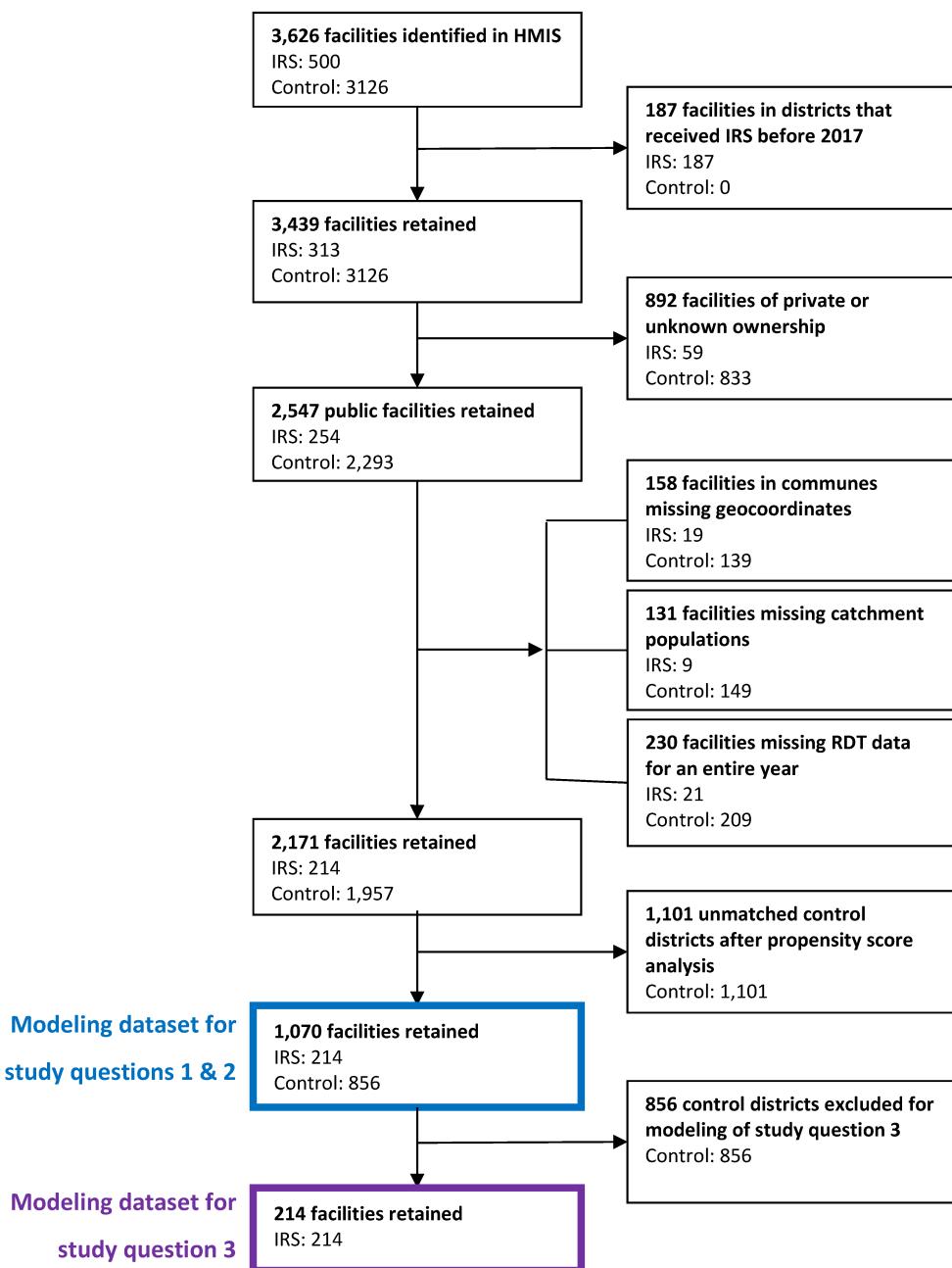
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## 1. Health facilities included in the study

Health facility data for all districts was obtained from the Madagascar DHIS2 for the period July 2016 to June 2021 and assessed for inclusion eligibility based on the following criteria:

1. Facilities in districts where IRS was implemented before 2017.
2. Non-public facilities (Hospitals and facilities owned/run by private/religious/NGO entities were excluded due to catchment population overlap with public primary facilities).
3. Facilities missing catchment population data in DHIS2.
4. Facilities in communes missing geocoordinates, which did not allow them to be linked to climate data.
5. Facilities missing RDT-confirmed case data for an entire year.

Following selection of facilities based on the above criteria, the remaining facilities were included in propensity score analysis (described in the next section) where facilities in control districts were matched to facilities in IRS districts. Unmatched control facilities were dropped from the analysis, and the remaining facilities were included in the modeling datasets used in study questions 1 and 2. The modeling dataset for study question 3 retained all IRS facilities and dropped all control facilities (Supplemental Figure 1).

**Supplemental Figure 1. Health facility eligibility and inclusion in the study.**

## 2. Propensity score analysis

Propensity score analysis is a method of matching untreated subjects to treated subjects based on even distribution of selected covariates.[1] Broadly, the steps for conducting propensity score analysis are:

1. Select the set of covariates to include.
2. Use logistic regression to obtain a propensity score for each subject.
3. Match exposed and unexposed subjects based on the propensity score.
4. Inspect the balance of covariates in exposed and unexposed groups after matching.

For this analysis, matching was performed at the health facility level using data from the first 12 months of the study period, (July 2016 to June 2017), before IRS had been implemented in any of the study districts. The selected covariates were: EVI, precipitation, ITN survival, and RDT-confirmed all ages malaria case incidence per 1,000 population. Covariates were averaged for each health facility over the 12-month period. Exposure to IRS was the binary outcome variable, where facilities where IRS would be implemented were assigned a 1, and control facilities were assigned a 0.

Control facilities were matched to IRS facilities based on nearest neighbor matching of propensity scores, with a 1:4 ratio of IRS to control. Each control facility could be matched to only one IRS facility.

A total of 856 control facilities were matched to 214 IRS facilities. Match quality was assessed based on comparisons of covariate distributions in control and IRS groups. For continuous covariates, the standard mean difference (SMD) was compared between groups for a threshold of 0.25. The SMD is calculated as:

$$SMD \text{ of } X = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{(Var_1 + Var_2)/2}}$$

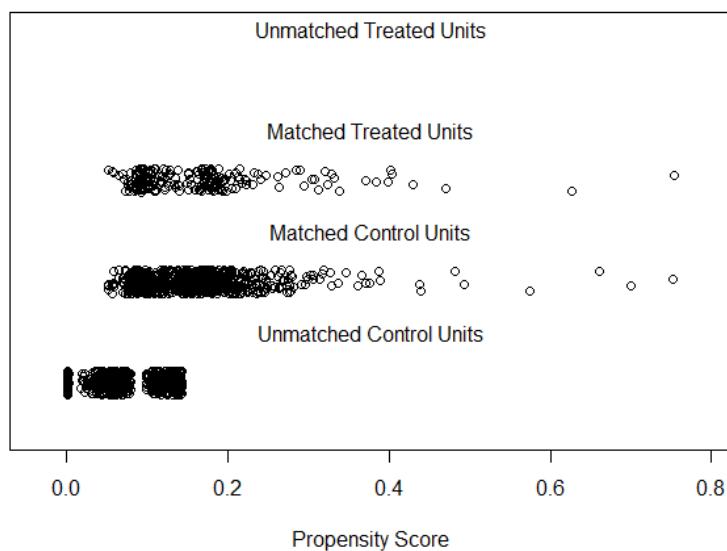
Where  $\bar{X}_1$  and  $\bar{X}_2$  are the sample means for the exposed and unexposed groups, respectively, and  $Var_1$  and  $Var_2$  are sample variances for the exposed and unexposed groups.[2]

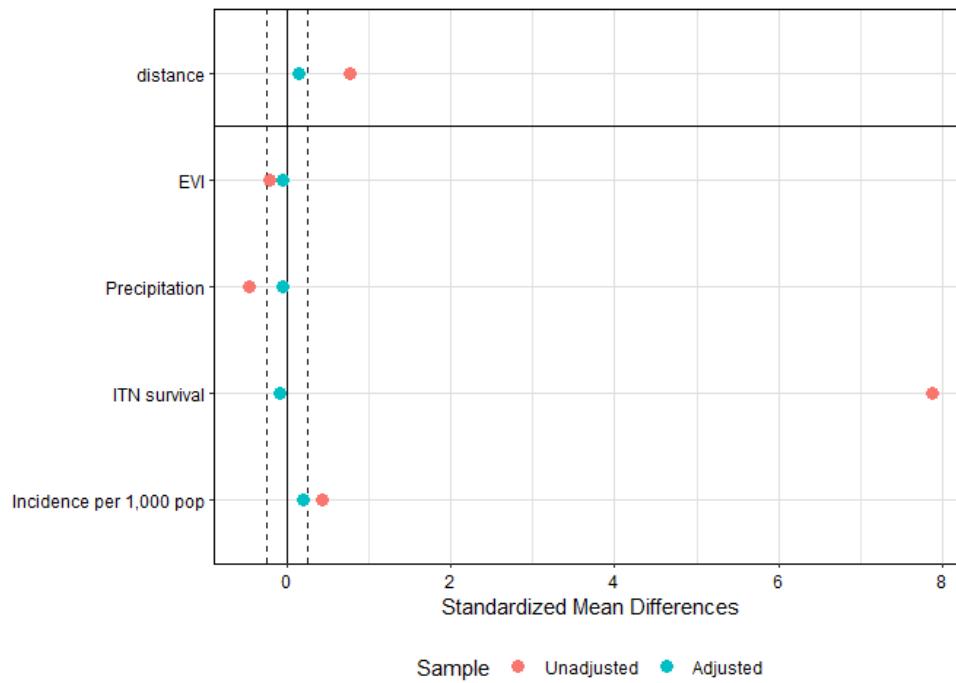
Diagnostic plots of matched IRS and control facilities are presented below.

**Supplemental Table 1. Number of IRS and control facilities matched via propensity score matching, per IRS study district.**

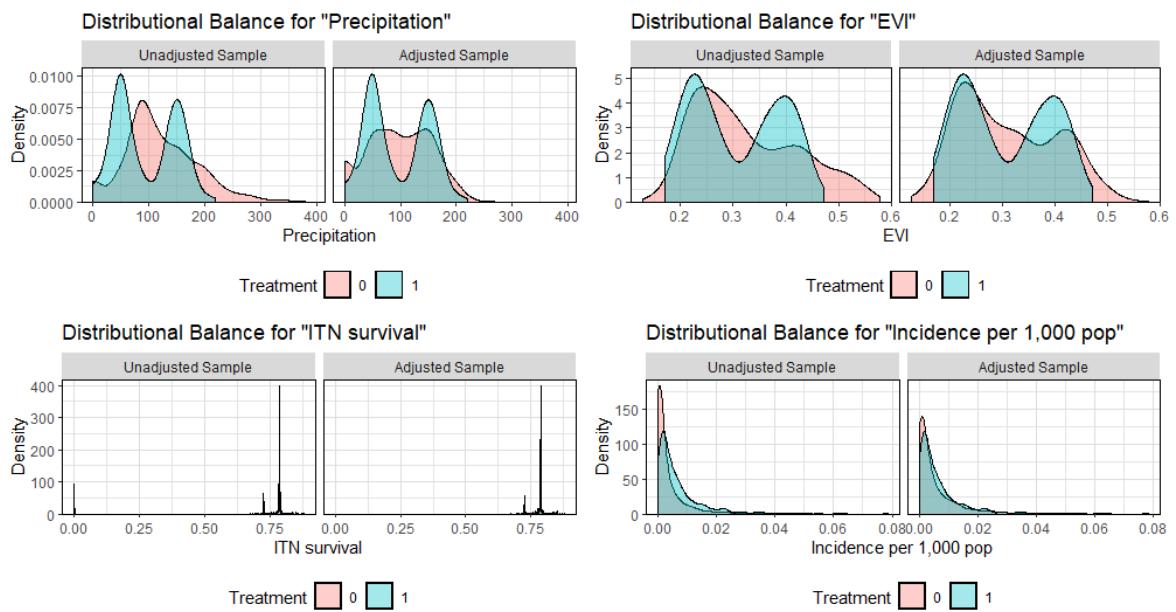
IRS district	IRS	Control
Ampanihy Ouest	23	92
Betioky Atsimo	26	104
Iakora	6	24
Ihosy	16	64
Manakara Atsimo	43	172
Mananjary	36	144
Sakaraha	12	48
Toliara II	33	132
Vondrozo	19	76
<b>Total</b>	<b>214</b>	<b>856</b>

**Supplemental Figure 2. Distribution of propensity scores for matched and unmatched facilities using 1:4 nearest neighbor matching without replacement on propensity score. Each circle represents one facility.**



**Supplemental Figure 3. Standardized mean differences (SMD) of covariates before and after matching.****Vertical dashed lines represent the 0.25 acceptable threshold.**

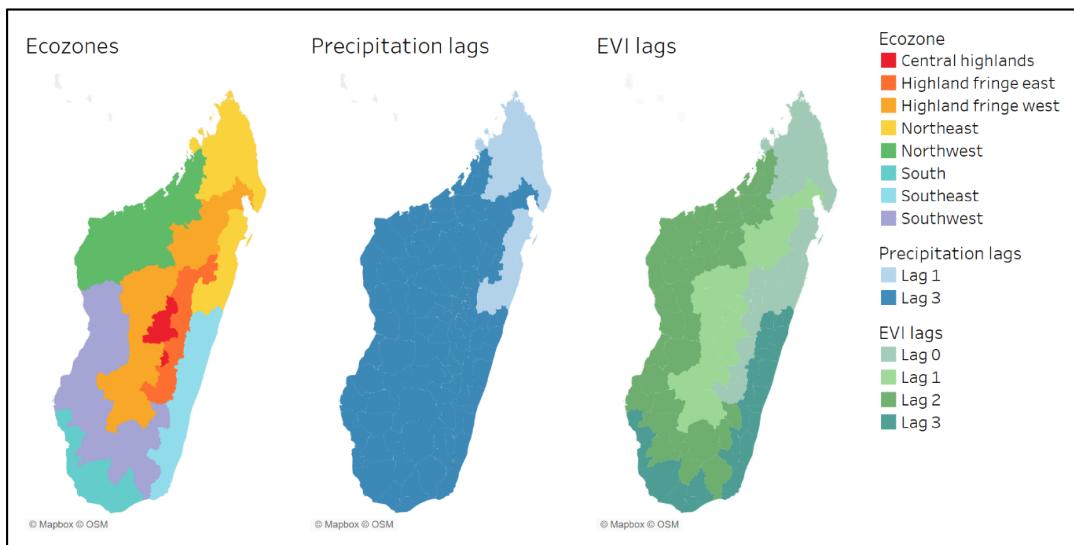
**Supplemental Figure 4. Distributional balances of covariates used in propensity score analysis before and after matching.**



### 3. Madagascar ecozones

To account for varying climate and transmission patterns across Madagascar, precipitation and enhanced vegetation index (EVI) were tested to determine the most appropriate lags for each district. Monthly precipitation and EVI were averaged over the eight malaria transmission ecozones identified by Howes et al.[3] and Pearson correlation tests were performed against monthly reported confirmed malaria cases. The selected lags, as well as a map of the eight ecozones are presented below.

***Supplemental Figure 5. Precipitation and enhanced vegetation index (EVI) lags most correlated with malaria cases in the eight distinct ecozones.***



#### 4. Coding of IRS exposure covariates

**Supplemental Table 2.** Sample table demonstrating how IRS exposure covariates in this study were coded. In this example, IRS was deployed in District A for the first time in October 2019. Blue columns were the exposure covariates included in the model for study question 1; red columns for study question 2; and green columns for study question 3.

District	Commune	Health facility	Year	Month	IRS status 0-6 months	IRS status 7-12 months	12 months post-IRS Year 1	12 months post-IRS Year 2	12 months post-IRS Year 3	IRS spray coverage <85%	IRS spray coverage 85-90%	IRS spray coverage 91-95%	IRS spray coverage 96-100%	IRS spray coverage – continuous	RDT-confirmed malaria cases	Other covariates...
A	A.1	A.1.1	2019	Jul	0	0	0	0	0	0	0	0	0	0	16	
A	A.1	A.1.1	2019	Aug	0	0	0	0	0	0	0	0	0	0	10	
A	A.1	A.1.1	2019	Sep	0	0	0	0	0	0	0	0	0	0	11	
A	A.1	A.1.1	2019	Oct	1	0	1	0	0	1	0	0	0	75%	42	
A	A.1	A.1.1	2019	Nov	1	0	1	0	0	1	0	0	0	75%	110	
A	A.1	A.1.1	2019	Dec	1	0	1	0	0	1	0	0	0	75%	31	
A	A.1	A.1.1	2020	Jan	1	0	1	0	0	1	0	0	0	75%	136	
A	A.1	A.1.1	2020	Feb	1	0	1	0	0	1	0	0	0	75%	39	
A	A.1	A.1.1	2020	Mar	1	0	1	0	0	1	0	0	0	75%	62	
A	A.1	A.1.1	2020	Apr	0	1	1	0	0	1	0	0	0	75%	29	
A	A.1	A.1.1	2020	May	0	1	1	0	0	1	0	0	0	75%	53	
A	A.1	A.1.1	2020	Jun	0	1	1	0	0	1	0	0	0	75%	67	
A	A.1	A.1.1	2020	Jul	0	1	1	0	0	1	0	0	0	75%	56	
A	A.1	A.1.1	2020	Aug	0	1	1	0	0	1	0	0	0	75%	17	
A	A.1	A.1.1	2020	Sep	0	1	1	0	0	1	0	0	0	75%	38	
A	A.1	A.1.1	2020	Oct	0	0	0	0	0	0	0	0	0	0	19	
A	A.1	A.1.1	2020	Nov	0	0	0	0	0	0	0	0	0	0	14	
A	A.1	A.1.1	2020	Dec	0	0	0	0	0	0	0	0	0	0	51	
A	A.2	A.2.1	2019	Jul	0	0	0	0	0	0	0	0	0	0	29	
A	A.2	A.2.1	2019	Aug	0	0	0	0	0	0	0	0	0	0	53	
A	A.2	A.2.1	2019	Sep	0	0	0	0	0	0	0	0	0	0	57	
A	A.2	A.2.1	2019	Oct	1	0	1	0	0	0	0	1	0	93%	66	
A	A.2	A.2.1	2019	Nov	1	0	1	0	0	0	0	1	0	93%	54	
A	A.2	A.2.1	2019	Dec	1	0	1	0	0	0	0	1	0	93%	32	
A	A.2	A.2.1	2020	Jan	1	0	1	0	0	0	0	1	0	93%	33	
A	A.2	A.2.1	2020	Feb	1	0	1	0	0	0	0	1	0	93%	11	
A	A.2	A.2.1	2020	Mar	1	0	1	0	0	0	0	1	0	93%	19	
A	A.2	A.2.1	2020	Apr	0	1	1	0	0	0	0	1	0	93%	39	
A	A.2	A.2.1	2020	May	0	1	1	0	0	0	0	1	0	93%	33	
A	A.2	A.2.1	2020	Jun	0	1	1	0	0	0	0	1	0	93%	35	

A	A.2	A.2.1	2020	Jul	0	1	1	0	0	0	0	1	0	93%	8	
A	A.2	A.2.1	2020	Aug	0	1	1	0	0	0	0	1	0	93%	4	
A	A.2	A.2.1	2020	Sep	0	1	1	0	0	0	0	1	0	93%	4	
A	A.2	A.2.1	2020	Oct	0	0	0	0	0	0	0	0	0	0	0	
A	A.2	A.2.1	2020	Nov	0	0	0	0	0	0	0	0	0	0	1	
A	A.2	A.2.1	2020	Dec	0	0	0	0	0	0	0	0	0	0	2	

## 5. Summary characteristics of study facilities

**Supplemental Table 3. Summary characteristics and indoor residual spraying (IRS) campaign results in the 9 IRS districts and their matched controls (matching performed by propensity score analysis) for the period July 2016 to June 2021.**

District		Number of health facilities	Transmission year*	All ages RDT-confirmed malaria cases	Population	Avg. EVI	Precipitation (mm)	Avg. MDA coverage	Avg. ITN survival	Dates of IRS campaign	IRS product deployed	Population protected by IRS	Structures sprayed	Structures found	District-level spray coverage
Ampanihy Ouest	IRS	23	2016-2017	2,733	299,785	0.2	12,217		0.78	Oct – Dec 2019	Pirimiphos-methyl	570,846	130,446	135,676	97.0%
			2017-2018	4,219	317,587	0.19	10,679		0.49						
			2018-2019	4,856	333,469	0.19	16,809		0.87						
			2019-2020	8,538	375,958	0.22	10,102		0.72						
			2020-2021	10,542	408,889	0.18	11,123	90.6%	0.43						
	Control	92	2016-2017	23,232	763,466	0.28	74,113		0.79						
			2017-2018	30,731	816,829	0.29	108,467		0.48						
			2018-2019	37,652	906,646	0.28	113,490		0.87						
			2019-2020	76,701	931,780	0.29	97,792		0.72						
			2020-2021	110,551	959,594	0.27	95,816	31.8%	0.43						
Betioky Atsimo	IRS	26	2016-2017	15,420	196,792	0.23	14,473		0.78	Oct – Dec 2019	Pirimiphos-methyl	273,856	66,590	69,679	96.4%
			2017-2018	16,564	214,160	0.21	12,370		0.48						
			2018-2019	18,265	229,151	0.22	19,799		0.87						
			2019-2020	15,904	257,062	0.24	12,748		0.72						
			2020-2021	13,789	284,309	0.21	13,957		0.43	Nov – Dec 2020	Pirimiphos-methyl	285,406	69,511	71,383	97.9%
	Control	104	2016-2017	40,946	754,142	0.27	60,719		0.79						
			2017-2018	63,871	809,501	0.28	83,793		0.48						
			2018-2019	54,894	925,836	0.27	93,620		0.87						
			2019-2020	98,799	954,368	0.28	80,156		0.72						
			2020-2021	158,792	975,177	0.26	103,276	30.9%	0.43						
Iakora	IRS	6	2016-2017	2,261	30,151	0.28	4,420		0.79						
			2017-2018	3,118	30,436	0.29	6,477		0.46						

			Year	Number of houses treated	Number of households	Prevalence (%)	Number of cases	Case fatality rate (%)	Intervention		Number of houses treated	Number of households	Prevalence (%)	Number of cases	Case fatality rate (%)
									Control	IRS					
			2018-2019	9,325	39,390	0.29	8,950	0.87							
			2019-2020	11,547	42,567	0.28	5,976	0.72							
			2020-2021	16,896	45,447	0.27	6,109	0.43	Nov 2020	Clothianidin/ deltamethrin	53,137	11,698	11,981	97.6%	
			2016-2017	10,054	229,034	0.27	22,640	0.78							
			2017-2018	15,781	251,335	0.27	30,443	0.49							
Control	24		2018-2019	17,180	268,404	0.26	30,321	0.87							
			2019-2020	26,108	276,315	0.27	27,547	0.72							
			2020-2021	35,865	284,982	0.25	27,164	20.4%		0.43					
			2016-2017	13,213	147,287	0.22	10,535	0.78							
IRS	16		2017-2018	30,164	173,002	0.2	10,991	0.49							
			2018-2019	16,822	201,560	0.21	14,853	0.87							
			2019-2020	18,173	237,910	0.19	10,571	0.72	Oct – Nov 2019	Pirimiphos-methyl & Clothianidin/ deltamethrin	200,563	42,911	44,617	96.5%	
			2020-2021	27,131	245,875	0.18	11,286	0.43	Nov – Dec 2020	Clothianidin/ deltamethrin	202,017	43,915	44,948	98.1%	
			2016-2017	17,708	502,458	0.26	47,236	0.79							
Ihosy	64		2017-2018	28,469	530,715	0.26	72,231	0.48							
			2018-2019	31,601	576,840	0.27	74,462	0.87							
			2019-2020	40,093	589,089	0.27	64,590	0.72							
			2020-2021	55,399	602,728	0.26	65,882	25.5%		0.43					
			2016-2017	10,256	324,215	0.39	74,529	0.79							
Manakara Atsimo	43		2017-2018	14,242	325,447	0.42	117,933	0.49	Jul 2017	Pirimiphos-methyl	315,258	72,450	78,928	92.4%	
			2018-2019	14,599	357,795	0.44	125,845	0.87	Jul 2018	Pirimiphos-methyl	345,104	76,379	86,314	89.1%	
			2019-2020	26,058	356,185	0.44	109,918	0.72							
			2020-2021	27,178	357,977	0.42	82,941	0.43							
			2016-2017	39,099	1,261,860	0.37	247,503	0.78							
Mananjary	IRS	36	2017-2018	56,640	1,408,655	0.37	362,453	0.49							
			2018-2019	58,155	1,486,693	0.37	343,680	0.87							
			2019-2020	111,292	1,452,343	0.38	314,687	0.72							
			2020-2021	174,141	1,432,328	0.37	276,288	8.5%		0.43					
			2016-2017	10,515	358,748	0.39	61,225	0.78							
			2017-2018	8,546	387,035	0.43	97,477	0.49	Jul 2017	Pirimiphos-methyl	249,597	58,464	62,074	94.3%	
			2018-2019	13,070	388,691	0.43	96,145	0.87	Jul 2018	Pirimiphos-methyl	279,822	65,245	69,561	94.2%	

			Year	Number of children treated	Number of children with fever	Proportion of children with fever (%)	Number of children with fever treated (%)						
			2019-2020	22,851	322,869	0.44	95,676	0.72					
			2020-2021	31,354	268,254	0.42	68,614	0.43					
			2016-2017	29,699	996,159	0.38	218,581	0.78					
			2017-2018	46,361	1,132,622	0.38	319,881	0.49					
Control	144	2018-2019	49,577	1,178,813	0.38	296,602	0.87						
		2019-2020	84,464	1,153,090	0.39	278,182	0.71						
		2020-2021	140,715	1,126,693	0.37	241,959	4.4%	0.43					
		2016-2017	16,324	110,769	0.22	6,710	0.79						
		2017-2018	13,302	117,650	0.2	6,181	0.49						
Sakaraha	12	2018-2019	12,690	127,361	0.21	9,757	0.87	Sep 2018	Pirimiphos-methyl	128,419	30,857	32,450	94.3%
		2019-2020	18,844	142,683	0.22	7,123	0.72	Oct – Nov 2019	Clothianidin	110,455	27,070	27,486	98.3%
		2020-2021	22,694	156,968	0.21	8,136	0.43	Nov – Dec 2020	Clothianidin	110,557	26,995	27,659	98.2%
		2016-2017	24,944	238,109	0.27	23,730	0.79						
		2017-2018	26,400	253,505	0.29	40,745	0.48						
Control	48	2018-2019	30,471	308,787	0.29	44,361	0.87						
		2019-2020	50,125	316,084	0.29	37,436	0.72						
		2020-2021	73,375	320,232	0.27	47,264	32.7%	0.43					
		2016-2017	22,032	193,123	0.26	12,176	0.77						
		2017-2018	17,596	234,259	0.21	9,166	0.49						
Toliara II	33	2018-2019	10,804	243,733	0.24	15,687	0.87	Jul 2018	Pirimiphos-methyl	402,343	96,335	110,118	86.5%
		2019-2020	19,936	281,781	0.25	10,926	0.72	Oct – Dec 2019	Clothianidin	243,637	58,937	62,930	95.2%
		2020-2021	24,741	320,085	0.22	16,156	0.43	Oct – Dec 2020	Clothianidin	256,403	63,653	65,751	97.6%
		2016-2017	44,413	990,562	0.27	86,060	0.79						
		2017-2018	59,264	1,104,097	0.28	129,551	0.48						
Control	132	2018-2019	64,256	1,243,304	0.28	134,808	0.87						
		2019-2020	102,508	1,302,374	0.29	116,407	0.72						
		2020-2021	167,837	1,331,847	0.27	133,577	31.7%	0.43					
		2016-2017	12,128	125,780	0.4	18,570	0.78						
		2017-2018	11,424	131,842	0.41	33,188	0.48	Jul 2017	Pirimiphos-methyl	125,374	27,690	29,203	94.8%
Vondrozo	IRS	2018-2019	20,805	139,759	0.42	37,047	0.87						

		2019-2020	38,724	155,179	0.43	28,605	0.72
		2020-2021	75,354	170,797	0.4	30,047	0.43
Control 73	2016-2017	19,396	577,723	0.31	76,189	0.78	
		28,432	632,720	0.31	121,053	0.48	
	2018-2019	26,927	699,788	0.31	117,264	0.87	
		60,914	721,666	0.31	106,429	0.72	
	2020-2021	93,310	739,243	0.3	101,653	14.3%	0.43

## 6. Statistical results of study question 1: Overall impact of IRS

**Supplemental Table 4. Full regression model coefficients, 95% confidence intervals (95%CI) and P-values describing the association between indoor residual spraying status 0–6 and 7–12 months post-campaign as categorical variables, and RDT-confirmed malaria cases among all ages.**

	IRR	95% CI		P
		Upper	Lower	
Cosine( $2\pi t/T$ )	1.048	1.028	1.067	0.000
Sine( $2\pi t/T$ )	0.653	0.583	0.732	0.000
<b>Transmission year</b>				
2016-2017	Ref			
2017-2018	1.096	1.016	1.183	0.018
2018-2019	1.498	1.398	1.605	0.000
2019-2020	1.945	1.816	2.083	0.000
2020-2021	2.286	2.112	2.474	0.000
<b>Transmission year ## Sine(<math>2\pi t/T</math>)</b>				
2016-2017	Ref			
2017-2018	1.586	1.511	1.664	0.000
2018-2019	1.622	1.548	1.700	0.000
2019-2020	1.129	1.077	1.184	0.000
2020-2021	1.423	1.358	1.492	0.000
<b>District</b>				
Ambalavao	Ref			
Ambanja	0.235	0.207	0.267	0.000
Ambatoboeny	0.322	0.280	0.371	0.000
Ambatofinandrahana	0.375	0.322	0.437	0.000
Ambatomainty	3.550	2.949	4.274	0.000
Ambatondrazaka	1.427	1.265	1.611	0.000
Ambilobe	1.007	0.837	1.211	0.945
Amboasary Sud	0.197	0.133	0.292	0.000
Ambovombe Androy	0.534	0.463	0.616	0.000
Ampanihy Ouest	1.692	1.288	2.222	0.000
Amparafaravola	0.912	0.749	1.112	0.364
Analalava	0.650	0.556	0.759	0.000
Andapa	1.070	0.940	1.217	0.306
Andilamena	1.694	1.436	1.998	0.000
Anjozorobe	0.190	0.163	0.223	0.000
Ankazoabo Atsimo	1.898	1.685	2.139	0.000
Ankazobe	2.151	1.870	2.473	0.000

Anosibe An'ala	0.038	0.032	0.046	0.000
Antanambao Manampontsy	2.532	2.098	3.057	0.000
Antsalova	0.597	0.523	0.681	0.000
Antsiranana II	1.013	0.885	1.160	0.847
Antsohihy	0.132	0.114	0.154	0.000
Bealanana	0.967	0.848	1.101	0.610
Befandriana Avaratra	0.299	0.203	0.439	0.000
Befotaka	1.136	0.996	1.296	0.058
Bekily	0.338	0.262	0.436	0.000
Belo Sur Tsiribihina	1.212	1.049	1.401	0.009
Beloha Androy	1.694	1.457	1.971	0.000
Benenitra	2.904	2.418	3.489	0.000
Beroroha	0.423	0.368	0.488	0.000
Besalampy	0.526	0.443	0.623	0.000
Betafo	2.432	2.060	2.871	0.000
Betioky Atsimo	2.247	1.952	2.586	0.000
Betroka	2.348	1.929	2.858	0.000
Boriziny Port Berge	1.153	0.993	1.338	0.063
Fenoarivobe	0.720	0.614	0.844	0.000
Iakora	0.644	0.560	0.739	0.000
Ifanadiana	1.150	1.025	1.291	0.017
Ihosy	0.845	0.727	0.983	0.029
Ikalamavony	1.700	1.444	2.002	0.000
Ikongo Fort_Carnot	2.085	1.738	2.501	0.000
Ivohibe	1.531	1.345	1.742	0.000
Kandreho	2.552	2.048	3.181	0.000
Maevatanana	1.355	0.909	2.018	0.136
Mahabo	0.040	0.023	0.069	0.000
Mahajanga I	1.145	0.985	1.330	0.078
Mahajanga II	2.052	1.779	2.367	0.000
Mahanoro	0.683	0.514	0.908	0.009
Maintirano	2.920	2.555	3.336	0.000
Mampikony	0.438	0.388	0.496	0.000
Manakara Atsimo	0.094	0.080	0.111	0.000
Mananara Avaratra	3.253	2.883	3.671	0.000
Mananjary	3.418	2.774	4.211	0.000
Mandoto	1.192	1.055	1.347	0.005
Mandrirtsara	0.757	0.646	0.887	0.001
Manja	1.059	0.935	1.199	0.366
Maroantsetra	2.058	1.726	2.454	0.000
Marolambo	0.057	0.049	0.067	0.000
Marovoay	4.772	3.790	6.010	0.000
Miandrivazo	0.185	0.162	0.213	0.000

Midongy du Sud	0.271	0.237	0.310	0.000
Mitsinjo	0.757	0.670	0.856	0.000
Morafenobe	2.366	1.996	2.805	0.000
Moramanga	1.646	1.443	1.879	0.000
Morombe	0.047	0.028	0.079	0.000
Morondava	0.391	0.343	0.445	0.000
Nosy Be	1.380	1.228	1.551	0.000
Nosy Boraha Sainte Marie	2.207	1.835	2.654	0.000
Nosy Varika	2.387	2.031	2.806	0.000
Sakaraha	0.751	0.604	0.935	0.010
Sambava	2.099	1.698	2.595	0.000
Soalala	0.760	0.640	0.904	0.002
Soanierana Ivongo	0.798	0.707	0.902	0.000
Taolagnaro	0.034	0.029	0.039	0.000
Toamasina I	0.696	0.579	0.835	0.000
Toliara I	1.832	1.541	2.177	0.000
Toliara II	0.660	0.580	0.751	0.000
Tsaratana	0.216	0.187	0.251	0.000
Tsihombe	1.771	1.556	2.015	0.000
Tsiroanomandidy	1.587	1.384	1.819	0.000
Vangaindrano	0.655	0.527	0.814	0.000
Vatomandry	1.459	1.276	1.669	0.000
Vavatenina	1.025	0.888	1.184	0.736
Vohimarina	1.987	1.684	2.343	0.000
Vondrozo	0.162	0.132	0.199	0.000

District ## Sine( $2\pi t/T$ )

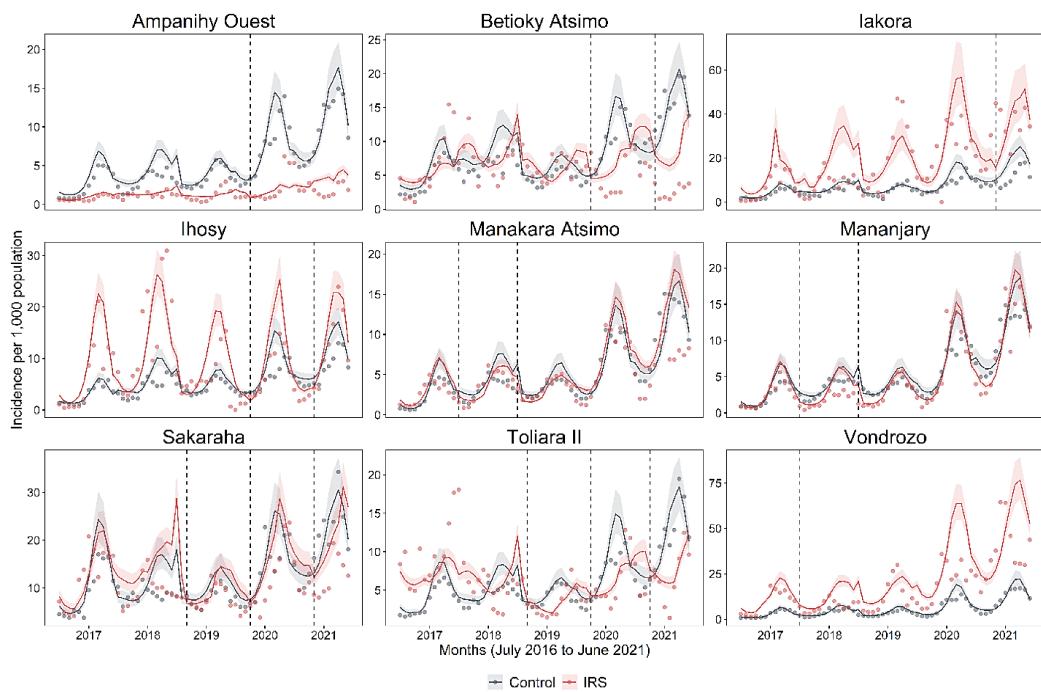
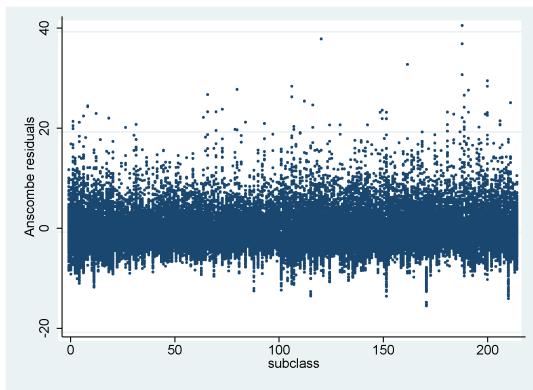
Ambalavao	Ref			
Ambanja	0.932	0.803	1.082	0.354
Ambatoboeny	1.293	1.105	1.513	0.001
Ambatofinandrahana	0.280	0.233	0.336	0.000
Ambatomaity	1.045	0.846	1.291	0.683
Ambatondrazaka	0.634	0.548	0.733	0.000
Ambilobe	1.039	0.835	1.292	0.734
Amboasary Sud	1.136	0.697	1.850	0.609
Ambovombe Androy	0.249	0.208	0.297	0.000
Ampanihy Ouest	0.514	0.358	0.737	0.000
Amparafaravola	0.318	0.250	0.404	0.000
Analalava	0.248	0.207	0.297	0.000
Andapa	0.572	0.497	0.659	0.000
Andilamena	0.453	0.369	0.557	0.000
Anjozorobe	1.225	1.028	1.460	0.023
Ankazoabo Atsimo	0.532	0.464	0.611	0.000

Ankazobe	0.962	0.817	1.132	0.641
Anosibe An'ala	0.805	0.640	1.013	0.065
Antanambao Manampontsy	0.912	0.729	1.141	0.421
Antsalova	0.765	0.657	0.891	0.001
Antsiranana II	0.391	0.337	0.453	0.000
Antsohihy	0.236	0.193	0.289	0.000
Bealanana	2.274	1.955	2.645	0.000
Befandriana Avaratra	1.304	0.806	2.110	0.280
Befotaka	1.742	1.494	2.031	0.000
Bekily	0.951	0.711	1.271	0.733
Belo Sur Tsiribihina	0.386	0.322	0.464	0.000
Beloha Androy	0.664	0.555	0.793	0.000
Benenitra	0.456	0.364	0.571	0.000
Beroroha	0.324	0.276	0.381	0.000
Besalampy	1.731	1.427	2.099	0.000
Betafo	0.908	0.744	1.107	0.339
Betioky Atsimo	0.771	0.655	0.908	0.002
Betroka	0.308	0.240	0.395	0.000
Boriziny Port Berge	0.284	0.239	0.338	0.000
Fenoarivobe	1.281	1.067	1.538	0.008
Iakora	0.908	0.772	1.068	0.244
Ifanadiana	1.304	1.139	1.494	0.000
Ihosy	1.499	1.255	1.791	0.000
Ikalamavony	0.420	0.344	0.512	0.000
Ikongo Fort_Carnot	1.040	0.842	1.286	0.714
Ivohibe	1.679	1.434	1.967	0.000
Kandreho	0.398	0.296	0.533	0.000
Maevatanana	0.910	0.549	1.507	0.713
Mahabo	0.927	0.460	1.865	0.831
Mahajanga I	0.904	0.761	1.075	0.253
Mahajanga II	0.886	0.753	1.044	0.149
Mahanoro	0.301	0.212	0.426	0.000
Maintirano	0.616	0.529	0.718	0.000
Mampikony	1.010	0.874	1.166	0.897
Manakara Atsimo	1.702	1.402	2.067	0.000
Mananara Avaratra	0.801	0.699	0.919	0.002
Mananjary	1.255	0.981	1.605	0.070
Mandoto	0.646	0.566	0.737	0.000
Mandritsara	0.369	0.311	0.437	0.000
Manja	0.477	0.417	0.545	0.000
Maroantsetra	1.103	0.893	1.362	0.363
Marolambo	0.760	0.623	0.926	0.007
Marovoay	0.921	0.698	1.214	0.557

Miandrivazo	0.992	0.847	1.162	0.919
Midongy du Sud	0.198	0.167	0.234	0.000
Mitsinjo	1.018	0.887	1.168	0.798
Morafenobe	1.100	0.897	1.350	0.361
Moramanga	0.428	0.366	0.500	0.000
Morombe	0.769	0.393	1.505	0.443
Morondava	0.323	0.275	0.379	0.000
Nosy Be	1.376	1.199	1.579	0.000
Nosy Boraha Sainte Marie	0.592	0.474	0.740	0.000
Nosy Varika	1.581	1.305	1.915	0.000
Sakaraha	0.643	0.506	0.817	0.000
Sambava	0.482	0.369	0.630	0.000
Soalala	1.164	0.954	1.419	0.135
Soanierana Ivongo	1.088	0.943	1.256	0.249
Taolagnaro	1.402	1.171	1.680	0.000
Toamasina I	0.392	0.318	0.482	0.000
Toliara I	1.048	0.858	1.281	0.645
Toliara II	0.433	0.368	0.510	0.000
Tsaratanana	1.434	1.208	1.702	0.000
Tsihombe	0.801	0.687	0.933	0.004
Tsiroanomandidy	1.312	1.117	1.541	0.001
Vangaindrano	0.429	0.337	0.545	0.000
Vatomandry	0.375	0.323	0.434	0.000
Vavatenina	0.597	0.510	0.699	0.000
Vohimarina	1.404	1.144	1.722	0.001
Vondrozo	0.306	0.237	0.395	0.000
<b>IRS exposure</b>				
0-6 months post-IRS	0.567	0.531	0.605	0.000
7-12 months post-IRS	0.752	0.704	0.802	0.000
<b>Precipitation (lagged and scaled)</b>				
EVI (lagged and scaled)	1.025	1.010	1.041	0.001
LLIN survival	1.143	1.113	1.174	0.000
MDA coverage	0.365	0.326	0.408	0.000
Observations	61,828			
Number of groups	214			

**Supplemental Figure 6. Study question 1 modeled estimates and residuals. (A) Modeled incidence of RDT-confirmed all-ages malaria incidence per 1,000 population in nine IRS districts from July 2016 to June 2017. Vertical dashed lines indicate the dates of IRS campaigns in each district. Solid lines represent modeled estimates and points represent observed values reported in DHIS2. Shading around the solid lines represent 95% confidence intervals of model estimates. (B) Plot of Anscombe's residuals.**

**(B) Plot of Anscombe's residuals by matched cluster.**

**A.****B.**

## 7. Statistical results of study question 2: Impact of sustained years of exposure to IRS

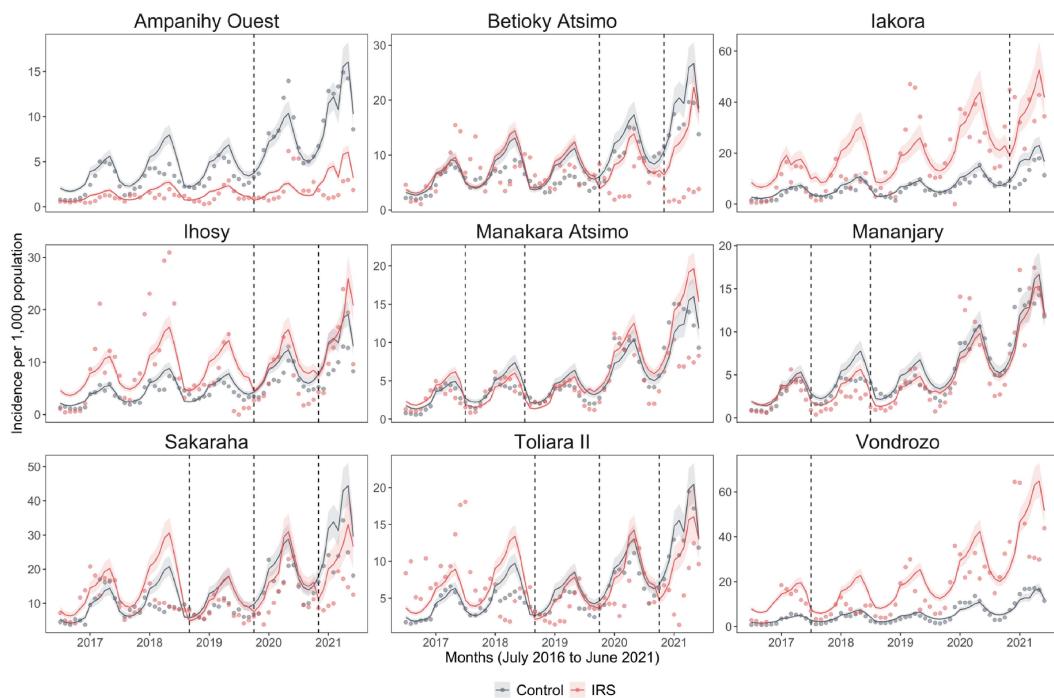
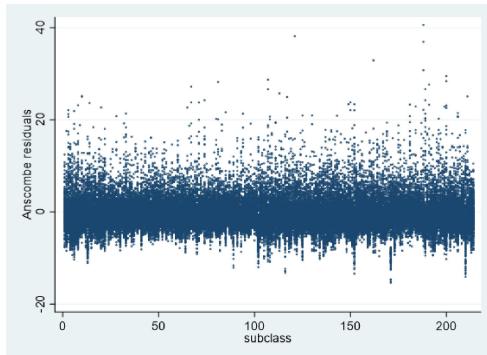
**Supplemental Table 5. Full regression model coefficients, 95% confidence intervals (95%CI) and P-values describing the association between indoor residual spraying status in the first, second, or third year of IRS implementation, and RDT-confirmed malaria cases among all ages.**

	IRR	95% CI		P
		Upper	Lower	
<b>Transmission year</b>				
2016-2017	Ref			
2017-2018	1.194	1.140	1.251	0.000
2018-2019	1.434	1.384	1.485	0.000
2019-2020	1.992	1.924	2.062	0.000
2020-2021	2.636	2.503	2.776	0.000
<b>Month</b>				
January	0.591	0.562	0.622	0.000
February	0.491	0.466	0.517	0.000
March	0.460	0.437	0.485	0.000
April	0.491	0.467	0.517	0.000
May	0.574	0.546	0.604	0.000
June	0.706	0.672	0.743	0.000
July	Ref			
August	1.048	0.997	1.100	0.064
September	1.146	1.089	1.206	0.000
October	1.320	1.249	1.396	0.000
November	1.361	1.289	1.436	0.000
December	1.058	1.003	1.117	0.038
<b>District</b>				
Ambalavao	Ref			
Ambanja	0.383	0.334	0.439	0.000
Ambatoboeny	0.518	0.442	0.607	0.000
Ambatofinandrahana	1.750	1.463	2.093	0.000
Ambatomainty	0.350	0.307	0.399	0.000
Ambatondrazaka	1.935	1.593	2.349	0.000
Ambilobe	0.315	0.278	0.356	0.000
Amboasary Sud	0.272	0.240	0.309	0.000
Ambovombe Androy	1.580	1.380	1.808	0.000
Ampanihy Ouest	0.170	0.149	0.193	0.000
Amparafaravola	0.309	0.273	0.349	0.000
Analalava	0.533	0.468	0.606	0.000
Andapa	1.536	1.299	1.817	0.000

Andilamena	0.318	0.247	0.408	0.000
Anjozorobe	0.959	0.834	1.104	0.560
Ankazoabo Atsimo	0.124	0.107	0.144	0.000
Ankazobe	1.556	1.349	1.796	0.000
Anosibe An'ala	0.524	0.461	0.595	0.000
Antanambao Manampontsy	0.763	0.664	0.876	0.000
Antsalova	1.030	0.858	1.236	0.751
Antsiranana II	2.130	1.820	2.493	0.000
Antsohihy	0.028	0.025	0.032	0.000
Bealanana	0.870	0.753	1.005	0.058
Befandriana Avaratra	0.148	0.131	0.167	0.000
Befotaka	0.616	0.556	0.682	0.000
Bekily	2.688	2.229	3.240	0.000
Belo Sur Tsiribihina	0.594	0.524	0.673	0.000
Beloha Androy	1.188	1.044	1.353	0.009
Benenitra	0.177	0.153	0.206	0.000
Beroroha	1.357	1.136	1.620	0.001
Besalampy	1.247	1.096	1.419	0.001
Betafo	0.677	0.569	0.804	0.000
Betioky Atsimo	0.185	0.152	0.225	0.000
Betroka	1.095	0.973	1.232	0.132
Boriziny Port Berge	0.981	0.864	1.114	0.766
Fenoarivobe	0.622	0.533	0.725	0.000
Iakora	1.456	1.103	1.922	0.008
Ifanadiana	1.811	1.507	2.177	0.000
Ihosy	1.300	1.141	1.481	0.000
Ikalamavony	1.347	1.180	1.537	0.000
Ikongo Fort_Carnot	1.400	1.187	1.650	0.000
Ivohibe	1.031	0.925	1.148	0.583
Kandreho	2.155	1.725	2.693	0.000
Maevatanana	3.324	2.647	4.175	0.000
Mahabo	1.809	1.537	2.131	0.000
Mahajanga I	0.787	0.689	0.898	0.000
Mahajanga II	0.181	0.120	0.271	0.000
Mahanoro	1.131	0.750	1.706	0.558
Maintirano	1.307	1.146	1.491	0.000
Mampikony	0.745	0.618	0.900	0.002
Manakara Atsimo	1.137	1.034	1.250	0.008
Mananara Avaratra	0.709	0.577	0.871	0.001
Mananjary	1.002	0.908	1.106	0.963
Mandoto	1.276	1.081	1.507	0.004
Mandritsara	0.488	0.434	0.549	0.000
Manja	1.270	1.113	1.449	0.000

Maroantsetra	0.720	0.583	0.890	0.002
Marolambo	1.524	1.357	1.712	0.000
Marovoay	2.615	2.118	3.227	0.000
Miandrivazo	0.477	0.415	0.548	0.000
Midongy du Sud	2.991	2.527	3.540	0.000
Mitsinjo	1.590	1.358	1.863	0.000
Morafenobe	1.869	1.573	2.220	0.000
Moramanga	0.458	0.400	0.525	0.000
Morombe	0.949	0.833	1.082	0.438
Morondava	0.800	0.691	0.926	0.003
Nosy Be	0.273	0.184	0.405	0.000
Nosy Boraha Sainte Marie	0.044	0.027	0.074	0.000
Nosy Varika	0.920	0.815	1.040	0.182
Sakaraha	1.524	1.321	1.758	0.000
Sambava	0.041	0.024	0.071	0.000
Soalala	2.700	2.247	3.245	0.000
Soanierana Ivongo	0.775	0.586	1.025	0.074
Taolagnaro	1.644	1.481	1.824	0.000
Toamasina I	0.032	0.027	0.039	0.000
Toliara I	0.090	0.075	0.107	0.000
Toliara II	0.973	0.869	1.090	0.636
Tsaratana	1.306	1.124	1.517	0.000
Tsihombe	0.042	0.036	0.049	0.000
Tsiroanomandidy	1.696	1.372	2.097	0.000
Vangaindrano	2.764	2.498	3.058	0.000
Vatomandry	0.791	0.690	0.907	0.001
Vavatenina	0.752	0.633	0.892	0.001
Vohimarina	0.166	0.144	0.192	0.000
Vondrozo	2.509	2.235	2.818	0.000
<b>IRS exposure</b>				
Year 1	0.629858	0.593584	0.668348	0
Year 2	0.597635	0.554576	0.644038	0
Year 3	0.422875	0.355057	0.503647	0
<b>Precipitation (lagged and scaled)</b>				
EVI (lagged and scaled)	0.980	0.964	0.995	0.012
LLIN survival	1.001	0.977	1.026	0.939
MDA coverage	0.532	0.477	0.593	0.000
<b>Observations</b>	61,828			
<b>Number of groups</b>	214			

**Supplemental Figure 7. Study question 2 modeled estimates and residuals. (A) Modeled incidence of RDT-confirmed all-ages malaria incidence per 1,000 population in nine IRS districts from July 2016 to June 2017. Vertical dashed lines indicate the dates of IRS campaigns in each district. Solid lines represent modeled estimates and points represent observed values reported in DHIS2. Shading around the solid lines represent 95% confidence intervals of model estimates. (B) Plot of Anscombe's residuals.**

**A.****B.**

## 8. Statistical results of study question 3: Impact of level of IRS spray coverage

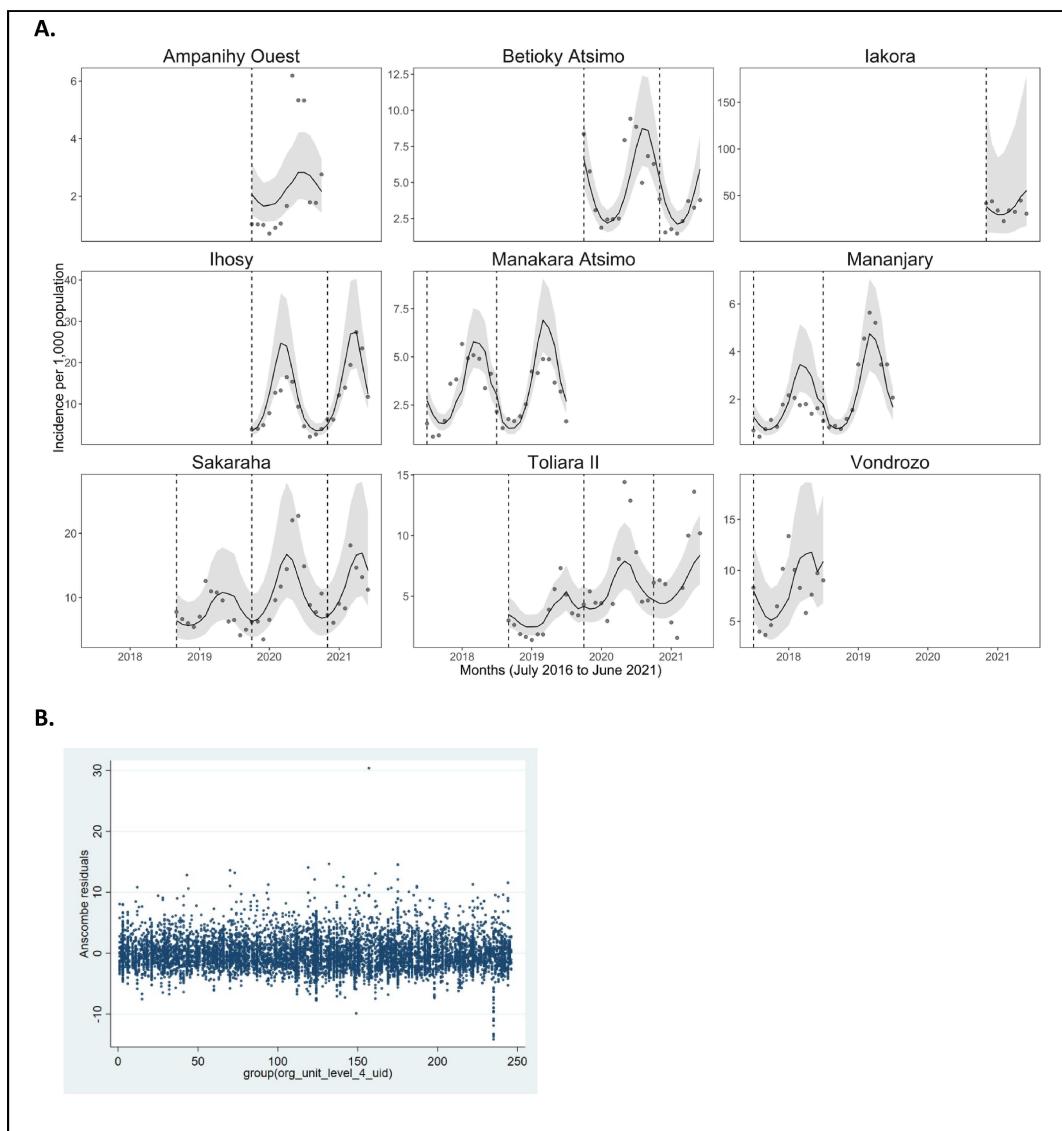
### 8.1. IRS spray coverage modeled as a categorical variable

**Supplemental Table 6. Full regression model coefficients, 95% confidence intervals (95%CI) and P-values resulting from a model describing the association between RDT-confirmed malaria cases among all ages and IRS spray coverage as a categorical variable with four coverage bins: ≤85%, 86%–90%, 91%–95%, and 96%–100%.**

	IRR	95% CI		P
		Upper	Lower	
Cosine( $2\pi t/T$ )	1.177	1.125	1.232	0.000
Sine( $2\pi t/T$ )	0.429	0.378	0.487	0.000
<b>Transmission year</b>				
2016-2017	Ref			
2017-2018	1.294	1.174	1.426	0.000
2018-2019	1.733	1.597	1.880	0.000
2019-2020	2.218	1.959	2.511	0.000
2020-2021	2.162	1.858	2.517	0.000
<b>Transmission year ## Sine(<math>2\pi t/T</math>)</b>				
2016-2017	Ref			
2017-2018	1.859	1.661	2.080	0.000
2018-2019	1.600	1.431	1.789	0.000
2019-2020	1.270	1.063	1.518	0.009
2020-2021	1.314	1.091	1.582	0.004
<b>District</b>				
Ampanihy Ouest	Ref			
Betioky Atsimo	0.585	0.315	1.086	0.089
Iakora	2.999	1.710	5.261	0.000
Ihosy	0.619	0.357	1.074	0.088
Manakara Atsimo	1.141	0.745	1.748	0.544
Mananjary	0.640	0.383	1.069	0.088
Sakaraha	1.044	0.594	1.836	0.881
Toliara II	2.629	1.543	4.479	0.000
Vondrozo	12.349	3.610	42.249	0.000
<b>District ## Sine(<math>2\pi t/T</math>)</b>				
Ampanihy Ouest	Ref			
Betioky Atsimo	0.533	0.451	0.630	0.000
Iakora	0.868	0.684	1.102	0.246
Ihosy	2.054	1.604	2.631	0.000

Manakara Atsimo	0.624	0.541	0.718	0.000
Mananjary	0.577	0.491	0.678	0.000
Sakaraha	0.629	0.544	0.727	0.000
Toliara II	0.719	0.572	0.905	0.005
Vondrozo	2.254	1.051	4.833	0.037
IRS spray coverage				
≤85%	Ref			
86-90%	0.803	0.690	0.934	0.005
91-95%	0.940	0.830	1.064	0.329
96-100%	1.070	0.944	1.214	0.289
Precipitation (lagged and scaled)	0.991	0.960	1.023	0.587
EVI (lagged and scaled)	1.185	1.101	1.274	0.000
LLIN survival	0.759	0.616	0.935	0.010
Observations	8,882			
Number of groups	246			

**Supplemental Figure 7. Study question 3 modeled estimates and residuals – IRS as a categorical variable. (A) Modeled incidence of RDT-confirmed all-ages malaria incidence per 1,000 population in nine IRS districts from July 2016 to June 2017 where IRS spray coverage is modeled as a categorical variable with four coverage bins: ≤85%, 86%–90%, 91%–95%, and 96%–100%. Data was restricted to include up to 12 months following each spray campaign. Vertical dashed lines indicate the dates of IRS campaigns in each district. Solid lines represent modeled estimates and points represent observed values reported in DHIS2. Shading around the solid lines represent 95% confidence intervals of model estimates. (B) Plot of Anscombe's residuals by commune.**



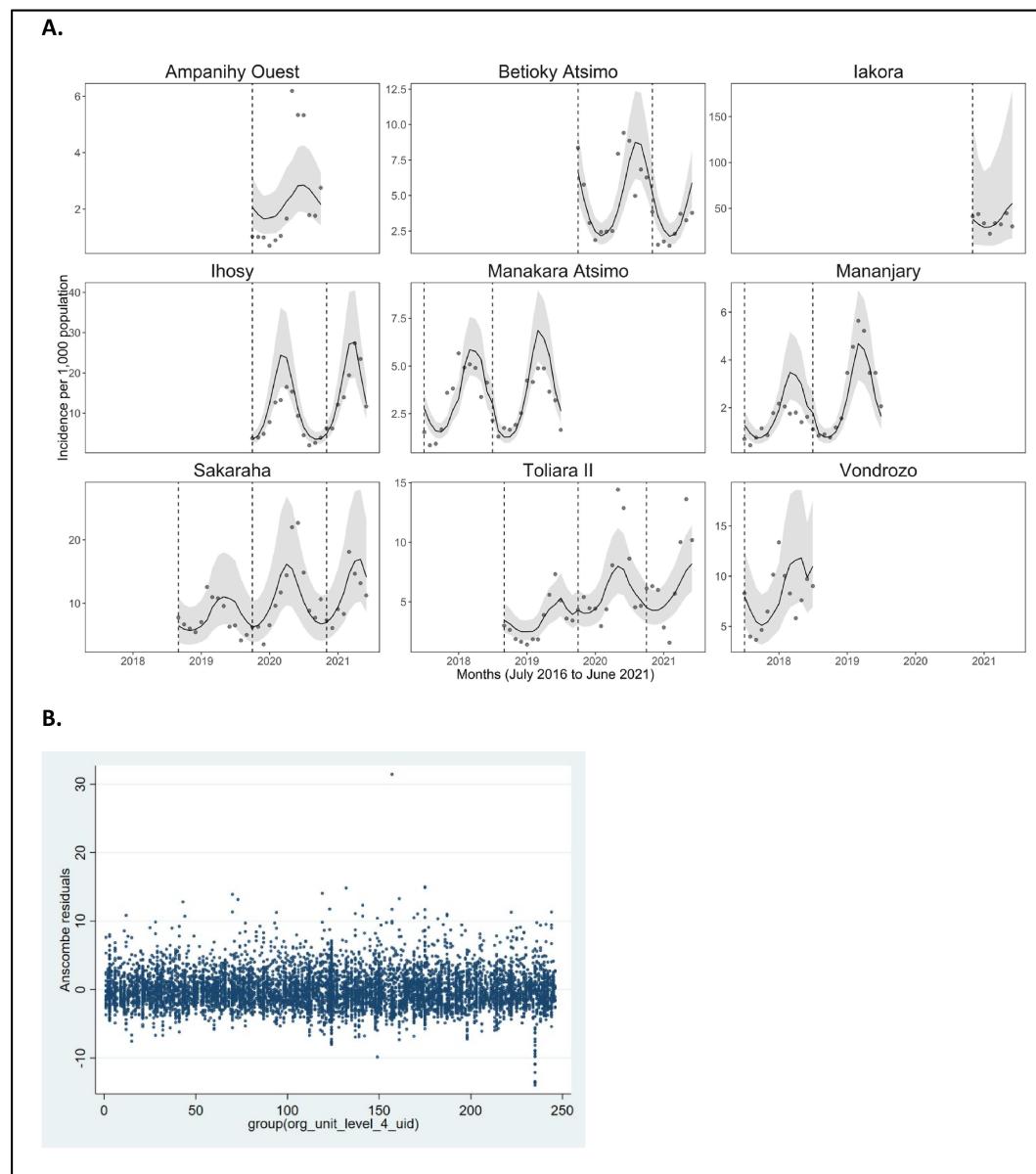
## 8.2. IRS spray coverage modeled as a continuous variable

**Supplemental Table 7. Full regression model coefficients, 95% confidence intervals (95%CI) and P-values resulting from a model describing the association between RDT-confirmed malaria cases among all ages and IRS spray coverage as a continuous variable.**

	IRR	95% CI		P
		Upper	Lower	
Cosine( $2\pi t/T$ )	1.175	1.123	1.230	0.000
Sine( $2\pi t/T$ )	0.430	0.378	0.488	0.000
<b>Transmission year</b>				
2016-2017	Ref			
2017-2018	1.302	1.182	1.435	0.000
2018-2019	1.756	1.619	1.904	0.000
2019-2020	2.200	1.946	2.488	0.000
2020-2021	2.186	1.881	2.540	0.000
<b>Transmission year ## Sine(<math>2\pi t/T</math>)</b>				
2016-2017	Ref			
2017-2018	1.864	1.665	2.086	0.000
2018-2019	1.604	1.434	1.794	0.000
2019-2020	1.301	1.089	1.555	0.004
2020-2021	1.313	1.090	1.582	0.004
<b>District</b>				
Ampanihy Ouest	Ref			
Betioky Atsimo	0.562	0.303	1.040	0.066
Iakora	2.979	1.703	5.212	0.000
Ihosy	0.624	0.361	1.080	0.092
Manakara Atsimo	1.115	0.730	1.704	0.615
Mananjary	0.622	0.373	1.036	0.068
Sakaraha	1.017	0.580	1.782	0.954
Toliara II	2.612	1.537	4.438	0.000
Vondrozo	12.463	3.661	42.424	0.000
<b>District ## Sine(<math>2\pi t/T</math>)</b>				
Ampanihy Ouest	Ref			
Betioky Atsimo	0.531	0.449	0.628	0.000
Iakora	0.864	0.681	1.098	0.231
Ihosy	2.003	1.564	2.565	0.000
Manakara Atsimo	0.620	0.538	0.714	0.000
Mananjary	0.576	0.490	0.677	0.000

Sakaraha	0.626	0.541	0.723	0.000
Toliara II	0.709	0.563	0.892	0.003
Vondrozo	2.254	1.050	4.836	0.037
IRS spray coverage	1.010	1.003	1.016	0.003
Precipitation (lagged and scaled)	0.992	0.961	1.024	0.615
EVI (lagged and scaled)	1.189	1.105	1.279	0.000
LLIN survival	0.747	0.607	0.921	0.006
Observations	8,882			
Number of groups	246			

**Supplemental Figure 8. Study question 3 modeled estimates and residuals – IRS as a continuous variable. (A) Modeled incidence of RDT-confirmed all-ages malaria incidence per 1,000 population in nine IRS districts from July 2016 to June 2017 where IRS spray coverage is modeled as a continuous variable. Data was restricted include up to 12 months following each spray campaign Vertical dashed lines indicate the dates of IRS campaigns in each district. Solid lines represent modeled estimates and points represent observed values reported in DHIS2. Shading around the solid lines represent 95% confidence intervals of model estimates. (B) Plot of Anscombe's residuals by commune.**



## 9. References

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